REMARKS

This paper is being filed in response to the Office Action dated July 27, 2004 that was issued in connection with the above-identified patent application. Following entry of the present Amendment, Claims 14-21, 23-26 and 28-38 are pending in the instant application. Claims 22 and 27 are cancelled and claims 35-38 have been added. Claims 14, 21, 28 and 32 have been amended. Claims 23-26, 29-31 and 34 are withdrawn. Withdrawn claims 23, 25, 26, 29 and 30 have also been amended, as discussed below. Pursuant to 37 C.F.R. §1.121(c)(2), these claims have been designated with the status identifier, "Withdrawn - Currently amended." The specification has also been amended, as discussed below. Support for all amendments and new claims can be found throughout the specification and claims as originally filed and there is no new matter added as a consequence of the amendments or new claims.

Request for Rejoinder

The Examiner has acknowledged that the subject matter presently under examination relates to methods of producing mature dendritic Langerhan's cells. As a result, the Examiner has withdrawn claims 23-26, 29-31 and 34 as being drawn to a non-elected invention. Claims 14-21, 28, 32, 33, 35-38 are under examination.

Applicants would like to thank the Examiner for the rejoinder of claims 32 and 33. However, applicants submit that the subject matter of withdrawn claims 23-26, 29-31 and 34, as amended, are also directed to methods of methods of producing *mature* dendritic Langerhan's cells. Since the withdrawn claims now recite *mature* dendritic Langerhan's cells, applicants submit that the newly added claims fall within the same invention as pending claims 14-21, 28, 32, 33 and 35-38 and respectfully request rejoinder of the withdrawn claims.

Objections to the Specification

The specification was objected to as failing to provide proper antecedent basis for the claimed subject matter for claims 14, 15, 17, 19, 20, 21 and 22. In response, the specification has been amended accordingly. Support for the amendments to the specification can be found throughout the specification as originally filed, and in particular, in the originally filed set of claims. Therefore, applicants request the withdrawal of the objections to the specification.

The Rejections under 35 U.S.C. § 112, ¶2 Should Be Withdrawn

Claims 14-22 and 27-28 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner points to the recitation of "dendritic Langerhans cells" rather than "mature dendritic Langerhans cells" in claims 14, 21, 22, 27 and 28. In response, applicants have amended claims 14, 21 and 28 to insert the reference to *mature* dendritic Langerhans cells. Therefore, applicants respectfully request the withdrawal of the rejection of claims under 35 U.S.C. § 112, second paragraph.

The Rejections under 35 U.S.C. § 112, ¶1 Should Be Withdrawn

Claims 14-22, 27-28, and 32-33 have been rejected under 35 U.S.C. §112, first paragraph, because the Examiner alleges that the specification does not contain a written description of the claimed invention. The Examiner alleges that the disclosure does not reasonably convey to the skilled artisan that the inventor had possession of the claimed invention at the time the application was filed. The Examiner alleges that there is no support for the use of mammalian platelets that result in mature dendritic Langerhans cells and the subject matter of claim 32, i.e. wherein more than about 50% of the mature dendritic

Langerhans cells have dendritic processes and display reactivity to anti-HLA-DR, anti-CD40, and anti-CD86 monoclonal antibodies and less than about 20% of the mature dendritic cells display reactivity to anti-CD1a, anti-CD80, and anti-CD83 monoclonal antibodies. The Examiner notes that upon careful review of the specification, there is allegedly no support for the use of mammalian platelets to produce mature dendritic Langerhans cells of any species or the use of specific results in generic claims. Applicants respectfully traverse this rejection.

With regard to claims 14 and 28, applicants submit that the claims, as amended herein, are fully supported by the application as filed. Claims 14 and 28 have been amended to recite the phrase, "wherein the platelets and the peripheral blood monocytes or bone marrow cells are derived from the same species or from phylogenetically close species." Support for the amendment to claims 14 and 28 can be found in the specification at page 3, lines 6 and 20. New claims 35 and 36 depend from claims 14 or 28 and are directed to platelets and monocytes or bone marrow cells being derived from human. Support for the new claims can be found in the specification at page 4, lines 6-9. New claims 37 and 38 depend from claims 14 or 28 and are directed to platelets and monocytes or bone marrow cells being derived from phylogenetically close species, rat and mouse.

With regard to claim 32, applicants submit that the claims, as amended herein, are fully supported by the application as filed. Claim 32, as amended, is directed to a method of producing mature *human* dendritic Langerhans cells using either *human* peripheral monocytes or *human* bone marrow cells and *human* platelets. Support for the amendment can be found in the specification beginning at page 7, line 21 to page 8, line 22. The results of the examples disclose that mature *human* dendritic Langerhans cells produced using the presently claimed method exhibit the claimed pattern of surface immunoreactivity.

For the foregoing reasons, applicants submit that the inventor had possession of the claimed invention and that there is sufficient written description of the claimed invention. Therefore, applicants respectfully request the withdrawal of the rejection of claims under 35 U.S.C. § 112, first paragraph.

The Rejections under 35 U.S.C. § 102(b) Should Be Withdrawn

Claims 14-17, 21, 28 and 32-33 are rejected under 35 U.S.C. § 102(b), as allegedly anticipated by Semple et al. ("Semple"). The Examiner alleges that Semple teaches a method for producing mature dendritic Langerhans cells, comprising selecting from the group consisting of peripheral blood monocytes and bone marrow cells in a medium containing mammalian platelets, and incubating the culture to enable formation of mature dendritic Langerhans cells, where the medium omits an exogenous cytokine, including GM-CSF or IL-4. The Examiner alleges that since the method steps of present invention are allegedly disclosed by Semple et al., the method taught by Semple inherently also produces mature dendritic Langerhans cells.

Applicants respectfully traverse these rejections. For a claim to be anticipated by a reference, "there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991). Moreover, a claim is anticipated and fails to meet the requirement of §102 only when a single prior art reference discloses each and every element of the claimed invention. *Lewmar Marine, Inc. v. Barient*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987), emphasis added.

The present invention is directed to methods of producing dendritic Langerhans cells from peripheral blood monocytes (PBMC) or bone marrow cells by incubating the PBMC

or bone marrow cells with platelets. The presence of platelets serve to replace the functional role of specific cytokines known to facilitate the development of mature dendritic Langerhans cells from PBMC or bone marrow cells. The replacement of cytokines with platelets is a significant cost-saving procedure.

In contrast to the present invention, Semple is primarily concerned with investigating the anti-platelet autoantibody activity associated with autoimmune thrombocytopenia (ATP). They observed that CD+ T helper cells from ATP patients, activated by platelets from a normal individuals, proliferate and secrete IL-2, which may modulate the anti-platelet activity. The reference also establishes the destruction of platelets, whereas the present invention is focused on the development of mature dendritic Langerhans cells using platelets, without destroying the platelets.

In addition, Semple fails to disclose the use of pure, isolated platelets. Experiments disclosed in Semple require the use of acid-washed platelets from normal human blood, which remove HLA antigens. For the present invention, the platelets are isolated using standard centrifugation to separate plasma (containing the platelets) from red blood cells, mononuclear cells, and neutrophils, followed by subjecting the plasma to high speed centrifugation to spin down the platelets. Since claims must be read in light of the specification's description, the platelets used in the present invention comprise a full spectrum of platelet surface antigens. The acid-wash step cited in Semple removes surface platelet antigens that may be necessary to facilitate the development of mature dendritic Langerhans cells from PBMC in the present invention. Applicants submit that, in the absence of some platelet surface antigens, the steps taught by Semple do not disclose each and every element of the claimed invention.

In relying upon the theory of inherency, the examiner must provide a basis in and/or technical reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teaching of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Int. 1990). Applicants assert that without the use of platelets, which are not acid-washed, the method taught by Semple would not produce a mature dendritic Langerhans cell and therefore the reference cannot inherently disclose the presently claimed invention.

For the foregoing reasons, applicants submit that the present invention is not anticipated by Semple and respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b).

The Rejections under 35 U.S.C. § 103(a) Should Be Withdrawn

Claims 18-20 have been rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Semple. The Examiner alleges that the only difference between the present invention and Semple is that Semple fails to teach the use of fetal calf serum. The Examiner further alleges that substitution of fetal calf serum for human serum and the determination of serum concentrations would be routine optimization.

Applicants respectfully disagree. To establish a *prima facie* case of obviousness, three basic criteria must be met (MPEP 2142). There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations. *In re Vaeck* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1981). Applicants submit, as discussed above, that Semple fails to disclose each and every limitation of the present invention.

Therefore, Semple does not render the claimed invention obvious. Applicants request withdrawal of the rejection of claims 18-20 under 35 U.S.C. § 103(a).

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request withdrawal of the outstanding rejections and allowance of the pending claims.

Applicants request a three month extension of time and enclose herewith the requisite fee as set forth in 37 C.F.R. § 1.17(a)(3). Applicants do not believe that any additional fee is required in connection with the submission of this document. However, should any fee be required, or if any overpayment has been made, the Commissioner is hereby authorized to charge any fees, or credit any overpayments made, to Deposit Account 02-4377. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

BAKER BOTTS, L.L.P.

Rochelle K. Seide
PTO Reg. No. 32,300
Attorney for Applicants

Dana Lau
PTO Reg. No. 55,361
Agent for Applicants

30 Rockefeller Plaza
New York, NY 10112
(212) 408-2500